


## Influenza Sequences 2



### Influenza Virus Resource

Information, Search and Analysis

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Multiple alignment for 11 nucleotide sequences. Alignment length is 1091.

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|           | 55  | 110       | 164       | 219       | 273       | 328       | 382       | 437       | 491       | 546       | 601       | 655     | 710    |
|-----------|---|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|---------|--------|
| Position. | .400.....   | .410..... | .420..... | .430..... | .440..... | .450..... | .460..... | .470..... | .480..... | .490..... | .500..... |         |        |
| Consensus | CCTGGAGTTTATCAATGAAGGCTTCAATTGGACTGGAGTCACTCAGAATGGGGGAAGCTATGCTTGCAAAAGGGGATCTGATAACAGTTTCTTTAGTAGATTG |           |           |           |           |           |           |           |           |           |           |         |        |
| KG_1968   | T.....  | C.....    | G.....    | T.....    | C.....    | G.....    | AG.....   | A.....    | T.....    | C.....    | G.....    | GC..... | C..... |
| NG_1972   | T.....  | G.....    | T.....    | C.....    | G.....    | A.....    | A.....    | A.....    | C.....    | G.....    | C.....    | C.....  | C..... |
| IC_1975   | T.....  | G.....    | T.....    | C.....    | G.....    | A.....    | AG.....   | A.....    | C.....    | G.....    | T.....    | C.....  | C..... |
| KS_1977   | T.....  | G.....    | T.....    | C.....    | G.....    | A.....    | A.....    | A.....    | C.....    | G.....    | C.....    | C.....  | C..... |
| HP_1982   | T.....  | G.....    | T.....    | C.....    | G.....    | A.....    | A.....    | A.....    | C.....    | G.....    | C.....    | C.....  | C..... |
| PG_1989   | T.....  | G.....    | T.....    | C.....    | G.....    | A.....    | A.....    | A.....    | C.....    | G.....    | C.....    | C.....  | C..... |
| AR_1992   | T.....  | G.....    | T.....    | C.....    | G.....    | A.....    | A.....    | A.....    | C.....    | G.....    | C.....    | C.....  | C..... |
| AD_1993   | T.....  | G.....    | T.....    | C.....    | G.....    | A.....    | A.....    | A.....    | C.....    | G.....    | C.....    | C.....  | C..... |
| DH_1997   | T.....  | G.....    | T.....    | C.....    | G.....    | A.....    | A.....    | A.....    | C.....    | G.....    | C.....    | C.....  | C..... |
| JK_1997   | T.....  | G.....    | T.....    | C.....    | G.....    | A.....    | A.....    | A.....    | C.....    | G.....    | C.....    | C.....  | C..... |
| IN_2003   | T.....  | G.....    | T.....    | C.....    | G.....    | A.....    | A.....    | A.....    | C.....    | G.....    | C.....    | C.....  | C..... |

The diagram above shows a multiple sequence alignment for the gene that codes for the hemagglutinin protein in 11 influenza viruses. Only 100 nucleotides from a total of over 1000 are shown. Samples are identified in the left column by country or city of origin and the year the virus was isolated from a patient. In this alignment, a "." means that the nucleotide is the same as the most common nucleotide in the sample. Nucleotides that remain the same in all samples have a darker grey background. Nucleotides that vary across the samples have a lighter background. Use the alignment to answer the following questions.

## Questions

1. Calculate the number of sites in the hemagglutinin gene that vary from nucleotide 399 and 499. The nucleotide number is located at the top of the alignment and is labeled “position.”
2. Calculate the number of changes per nucleotide in this 100 nucleotide sequence per year using the following formula.

$$\frac{\text{number of nucleotides that have at least one change}}{\left( \frac{\text{total number of nucleotides}}{\text{total number of years}} \right)}$$

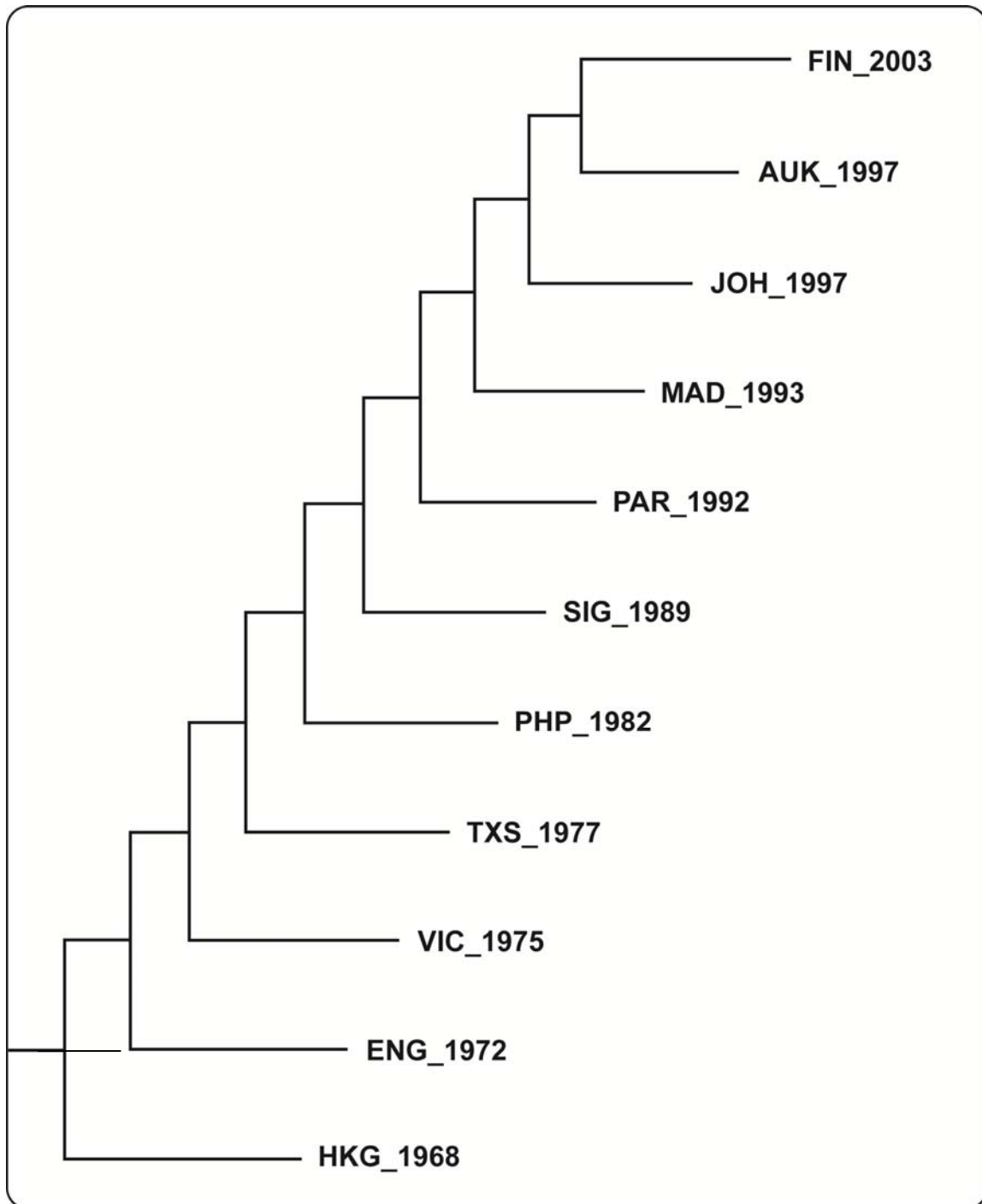
3. In Lesson 3, you investigated a portion of the sequence of a gene called IRF6 that is involved in the development of the head and face. You compared the sequence of this gene in many different species. 30 nucleotides from the IRF6 sequence are shown below.

**TGGGCCACcAGCCAGGGCTTtAGcCGgACT**

The lowercase grey letters show nucleotides that differ among some of the species. The uppercase black letters did not change. The amount of time represented in this comparison is 995 million years. Calculate the expected number of changes per nucleotide in this sequence per year.

4. Compare the rate of change per nucleotide per year for the hemagglutinin gene in influenza to the IRF6 gene. Do this by dividing the rate for the hemagglutinin region by the rate for the IRF6 gene. The number you calculate will show how many times faster one region changes compared to the other.
5. Previously in this lesson, you wrote down and shared your ideas about why the flu vaccine needs to be reformulated every few years. Use what you observed and learned so far in this activity revise and improve the explanation you gave previously.

### ***Relationships among Influenza Viruses***



This diagram shows the relationships among the influenza viruses sampled over 35 years. The length of the lines is an indication of the number of changes among the sequences. Each sample is named for the place and the year in which the virus was isolated from a patient. FIN = Finland, AUK = Auckland, JOH = Johannesburg, MAD = Madrid, PAR = Paris, SIG = Signapore, PHP = Philippines, TXS = Texas, VIC = Victoria, ENG = England, HKG = Hong Kong.

## ***Influenza and the Immune System***

### ***How your body fights influenza***

Influenza is a respiratory illness. The virus can infect the cells that line the lungs, nose, and throat. To infect your cells, the virus first needs to enter the cells. To enter a cell, the hemagglutinin protein on the virus binds to a receptor on your cells. Binding of the virus to your cell causes the cell to undergo endocytosis. Once inside, the virus starts replicating. Viruses use the “machinery” of the host cell to make new copies of their genetic material and to make proteins. These parts are assembled into a large number of new viruses.

One important way that your body fights influenza infections is by developing antibodies to the hemagglutinin on the virus. When antibodies attach to hemagglutinin, it keeps the virus from attaching to healthy cells which keeps them from infecting these cells.

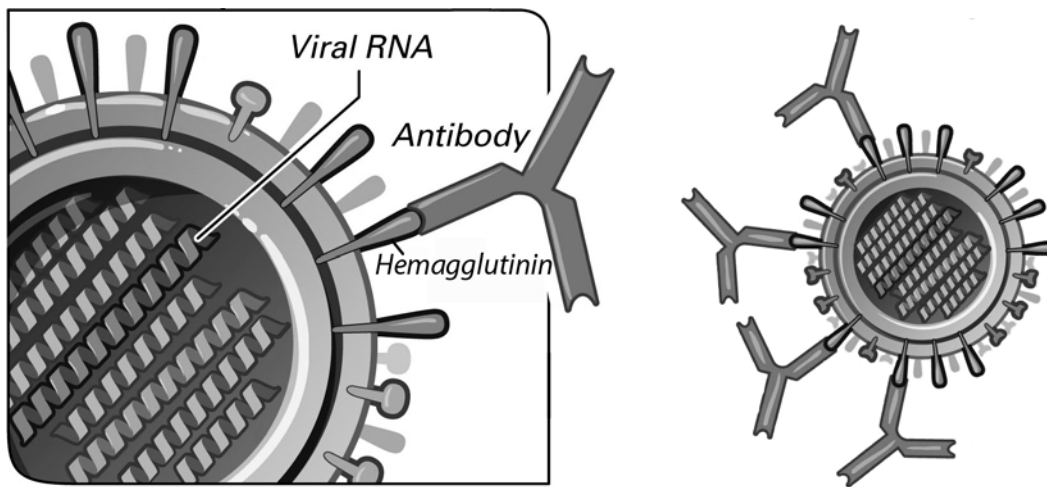


Image credit: National Institute of Allergy and Infectious Diseases (NIAID)

### ***Influenza, the immune system, and natural selection***

Scientists explored changes in the hemagglutinin gene in many influenza viruses that circulated around the world. Some mutations resulted in changes that affect how hemagglutinin binds to cell receptors. Because these changes affected the phenotype, it affected the ability of a virus to infect a cell.

Other mutations did not cause a change in amino acids. The protein that gets made from the gene is the same. The ability of these viruses to infect cells is not changed. As a result, these changes are mostly “invisible” to the process of natural selection.

Scientists compared the number of mutations that cause amino acid replacements to those that do not cause replacements. They found that there was a higher number of mutations that cause amino acid replacements than expected. This helped scientists conclude that the influenza virus seems to be evolving by natural selection to avoid detection by the immune system. This is part of the reason that the population of influenza viruses changes over time.

### Questions

1. Describe how a change in the gene for hemagglutinin in influenza could change the ability of an antibody from a person to bind to the virus.
2. Imagine an influenza virus that has a mutation that changes the shape of its hemagglutinin protein so antibodies made by a person no longer bind to the virus. A second virus does not have the mutation and antibodies from a person can bind to its hemagglutinin protein. Which virus would leave more descendants? Describe why you answered as you did.
3. How does learning about the immune system help explain the rapid rate of change in the hemagglutinin sequences you observed?
4. When you receive an influenza vaccine, you develop antibodies to the hemagglutinin protein for the strains of virus included in the vaccine. Use what you learned in this portion of the activity to revise and improve the explanation you gave previously about why the flu vaccine needs to be reformulated every few years.